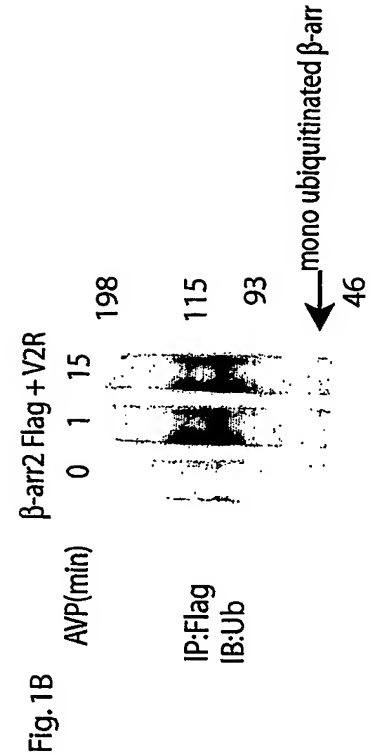


Fig. 1B

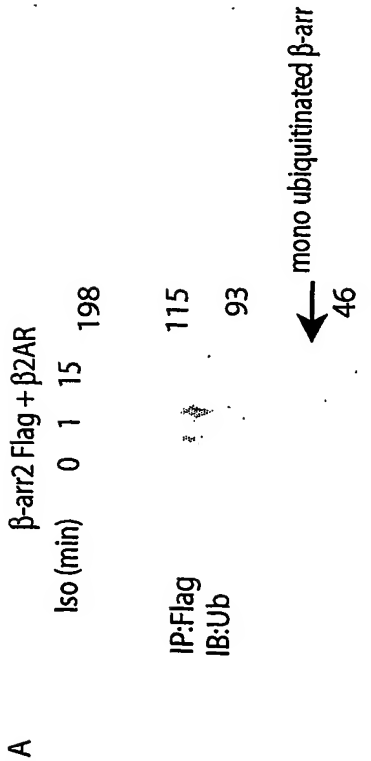


Fig. 1A

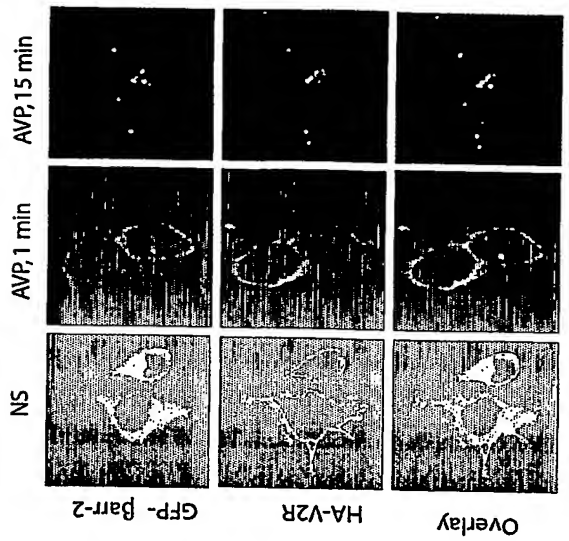


Fig. 1D

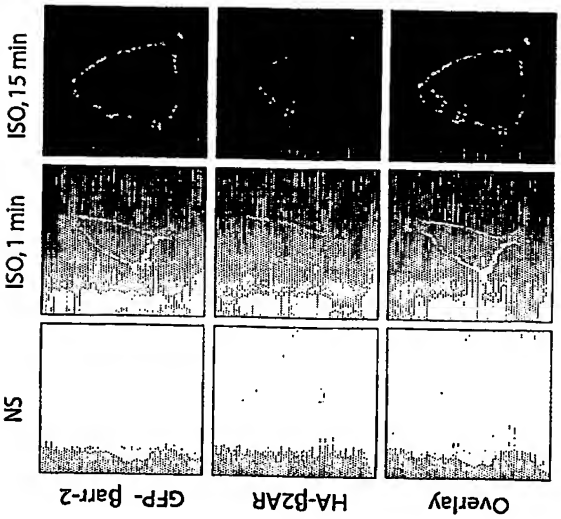


Fig. 1C

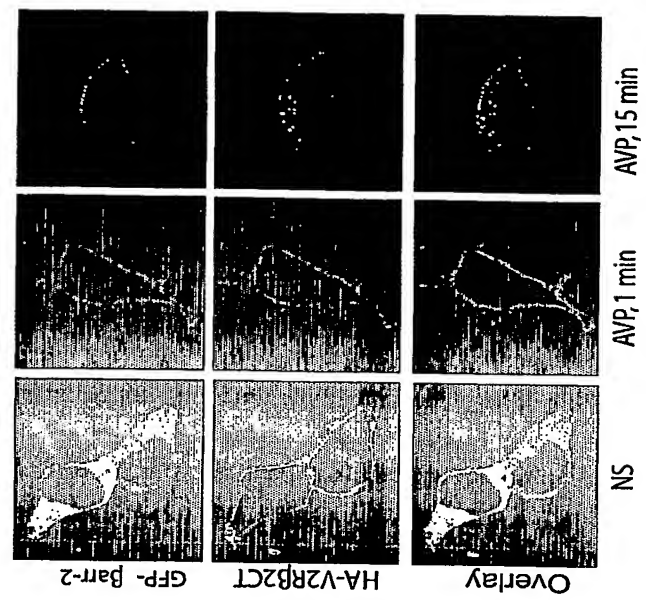


Fig. 2A

Fig. 2B

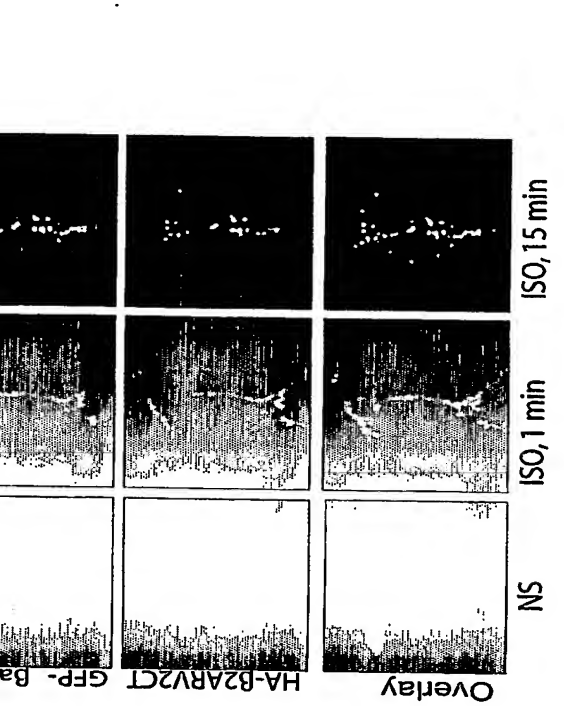


Fig. 2C

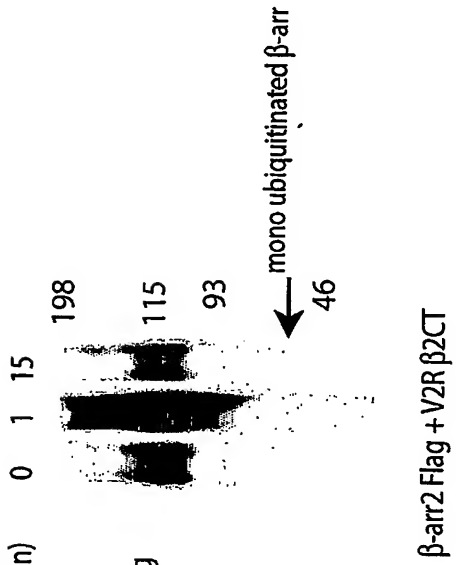
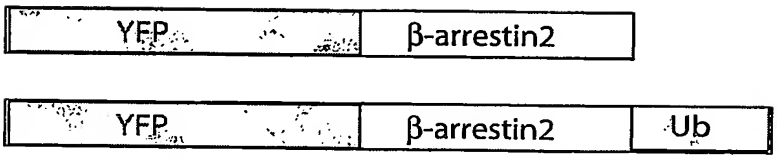
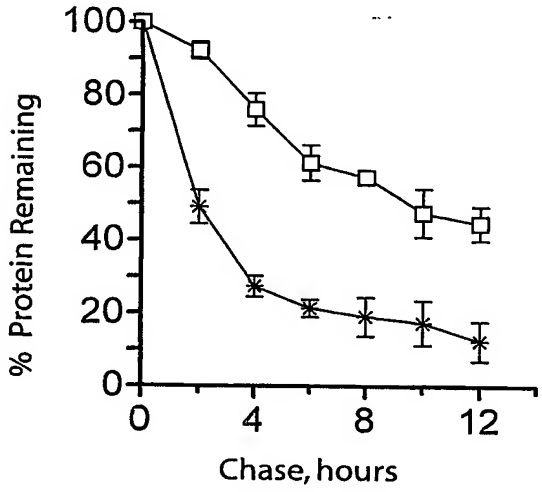


Fig. 2D

Fig. 3A


YFP
β-arrestin2
YFP
β-arrestin2
Ub


100
80
60
40
20
0
% Protein Remaining
0
4
8
12
Chase, hours

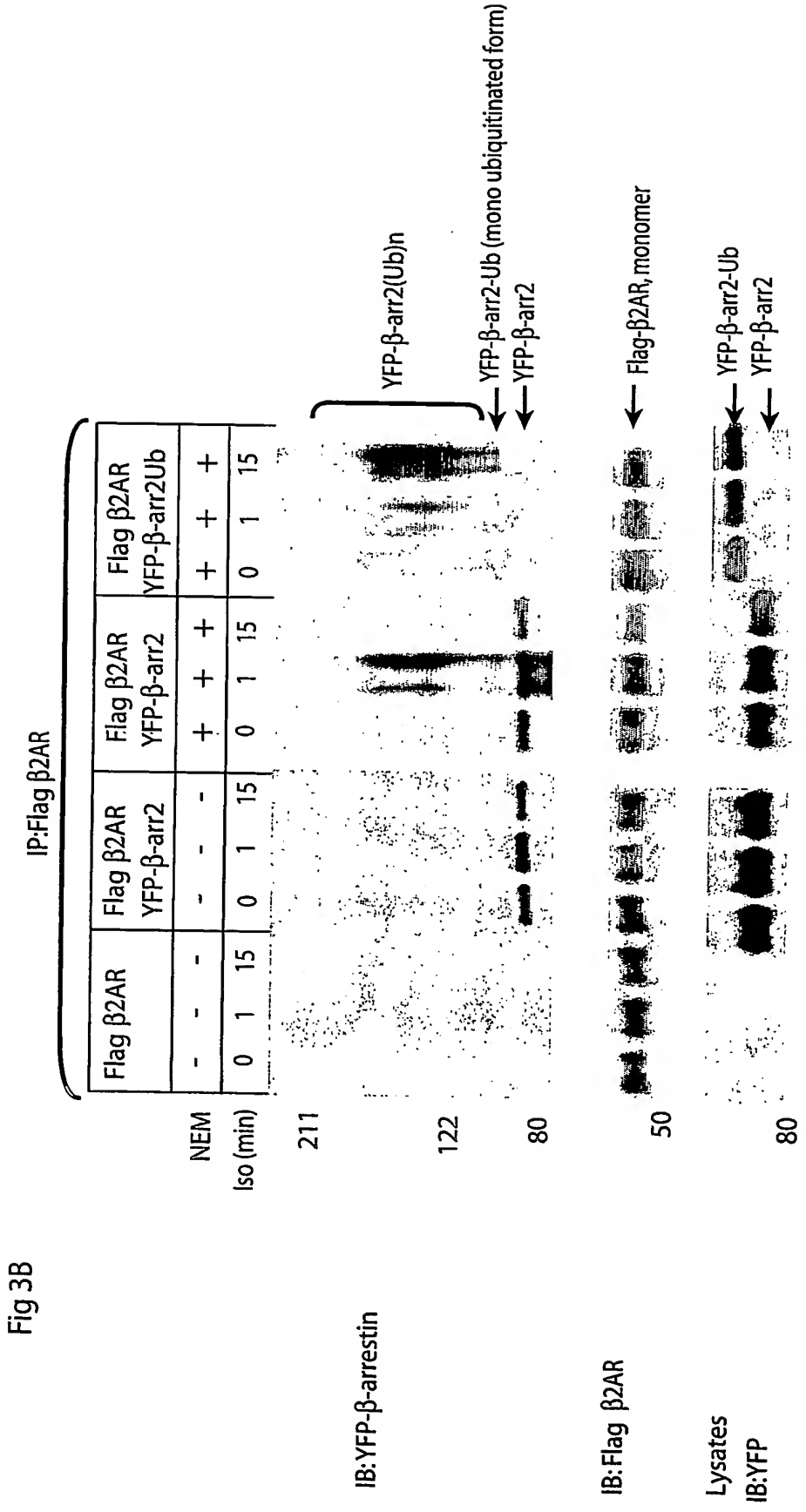

IP:Flag β2AR
Flag β2AR
Flag β2AR YFP-β-arr2
Flag β2AR YFP-β-arr2
Flag β2AR YFP-β-arr2Ub
NEM
Iso (min)
0 1 15 0 1 15 0 1 15 0 1 15
- - - - - - + + + + + +
IB:YFP-β-arrestin
YFP-β-arr2(Ub)n
YFP-β-arr2-Ub (mono ubiquitinated form)
YFP-β-arr2
211
122
80
IB:Flag β2AR
Flag-β2AR, monomer
50
Lysates
IB:YFP
YFP-β-arr2-Ub
YFP-β-arr2
80

Fig 3B

Fig. 4A

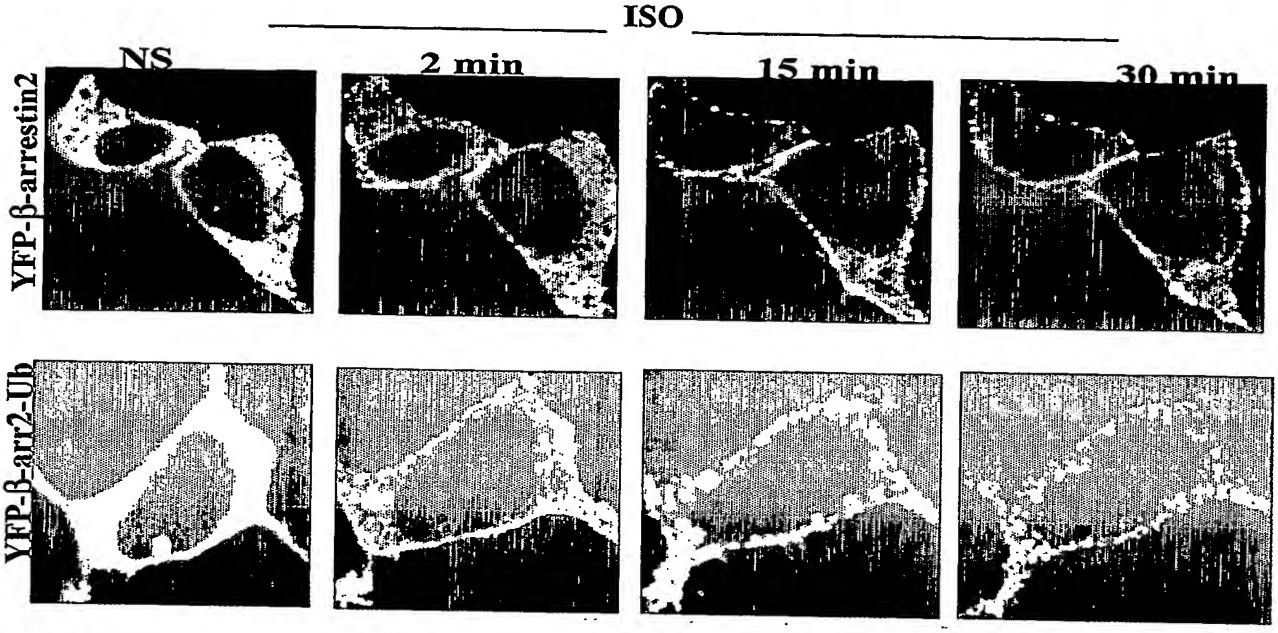

ISO
NS
2 min
15 min
30 min
YFP-β-arrestin2
YFP-β-arr2-Ub

Fig. 4B

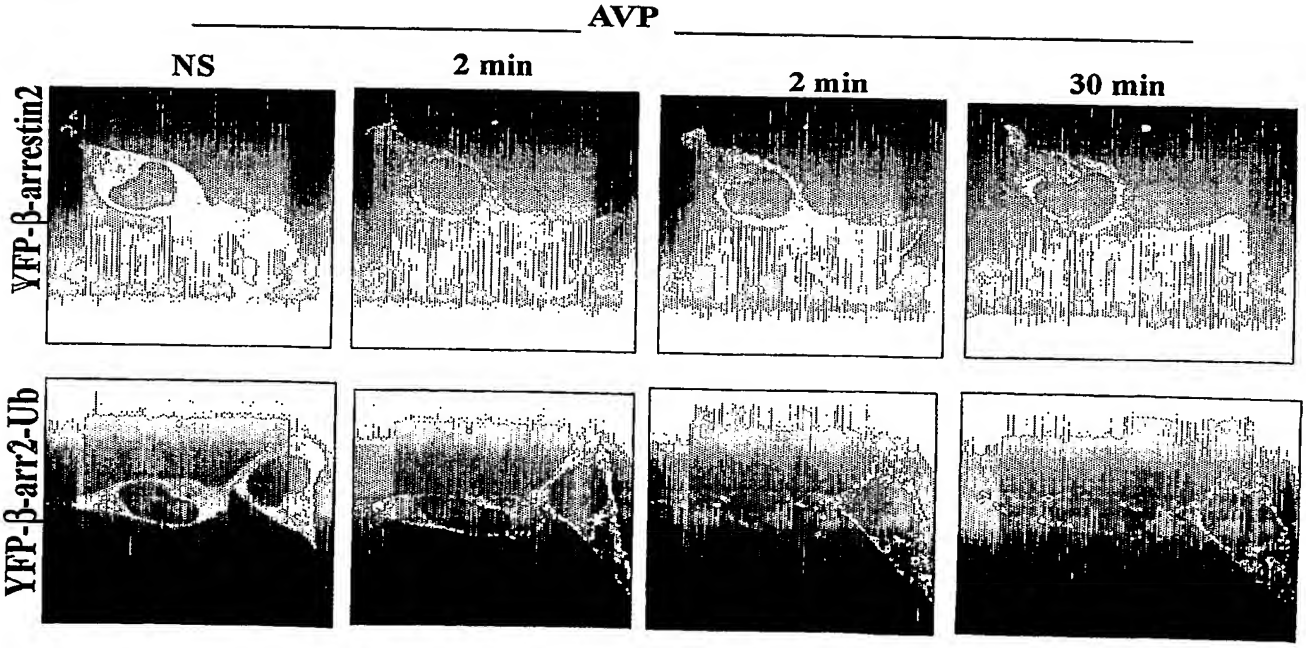

AVP
NS
2 min
2 min
30 min
YFP-β-arrestin2
YFP-β-arr2-Ub

Fig 5A

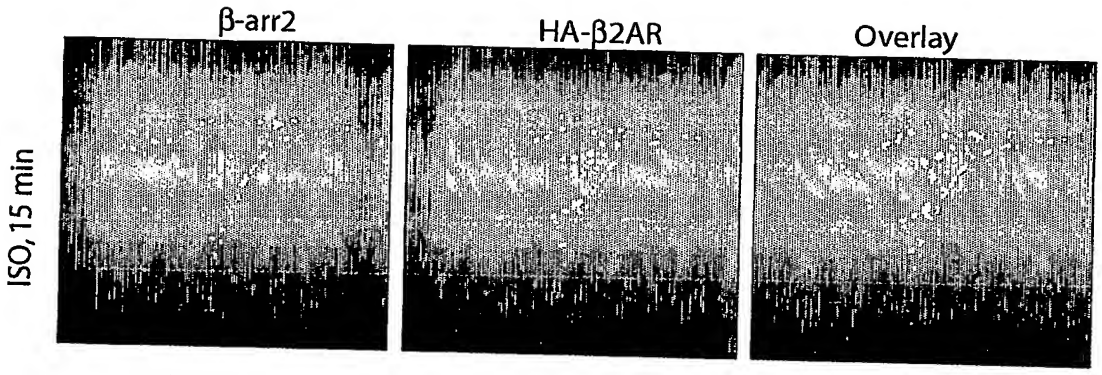

β-arr2
HA-β2AR
Overlay
ISO, 15 min

Fig 5B

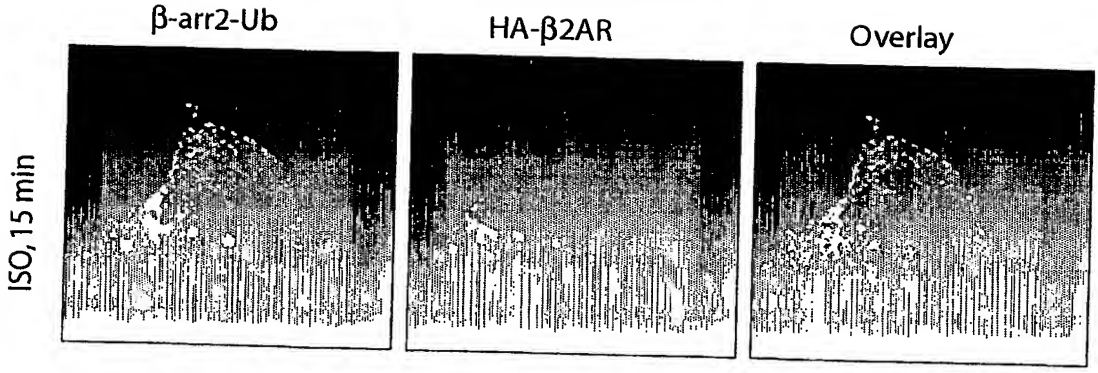

β-arr2-Ub
HA-β2AR
Overlay
ISO, 15 min

Fig. 6A

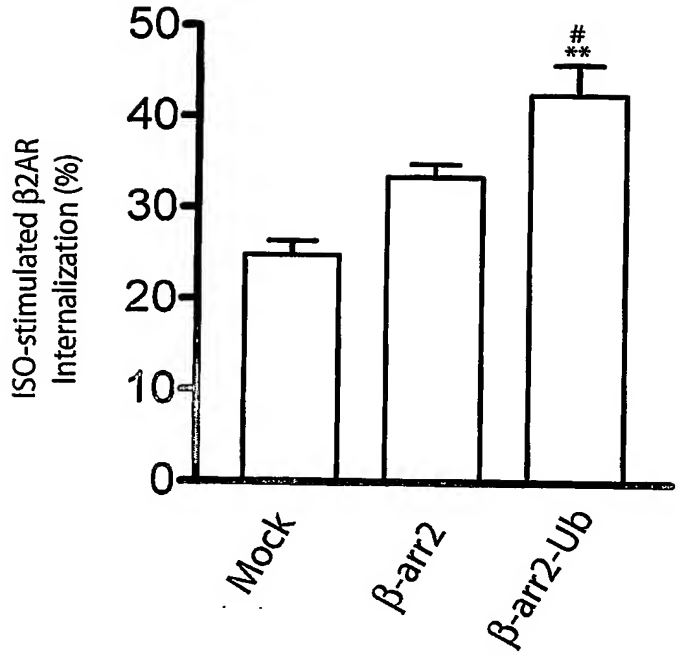

ISO-stimulated β2AR Internalization (%)
50
40
30
20
10
0
#
**
Mock
β-arr2
β-arr2-Ub

Fig. 6B

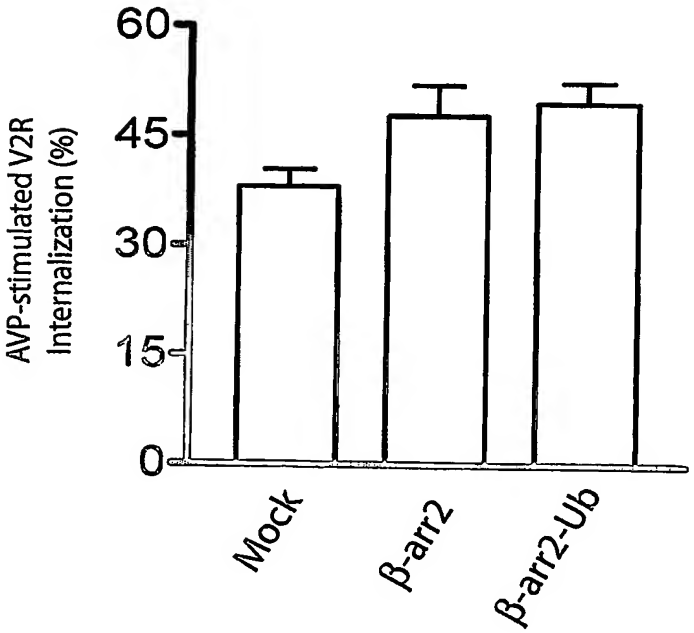

AVP-stimulated V2R Internalization (%)
60
45
30
15
0
Mock
β-arr2
β-arr2-Ub

Fig. 7A

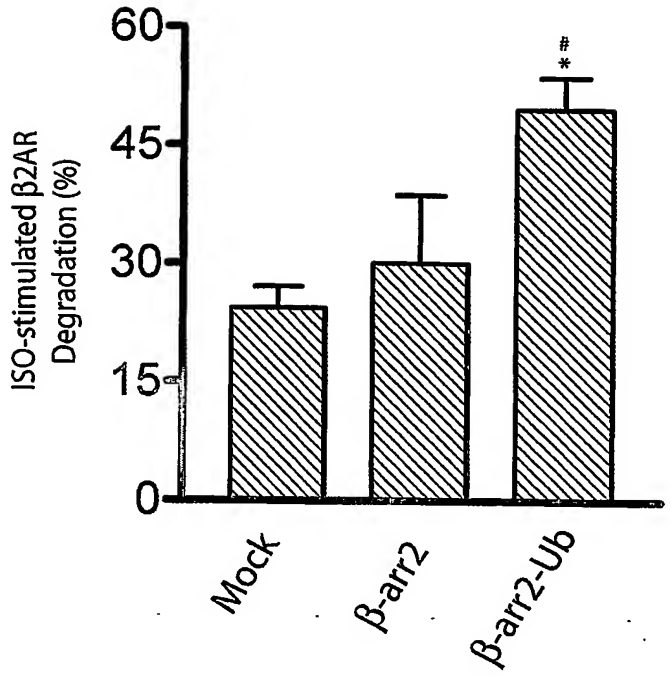

60
45
30
15
0
ISO-stimulated β2AR Degradation (%)
#
*
Mock
β-arr2
β-arr2-Ub

Fig. 7B

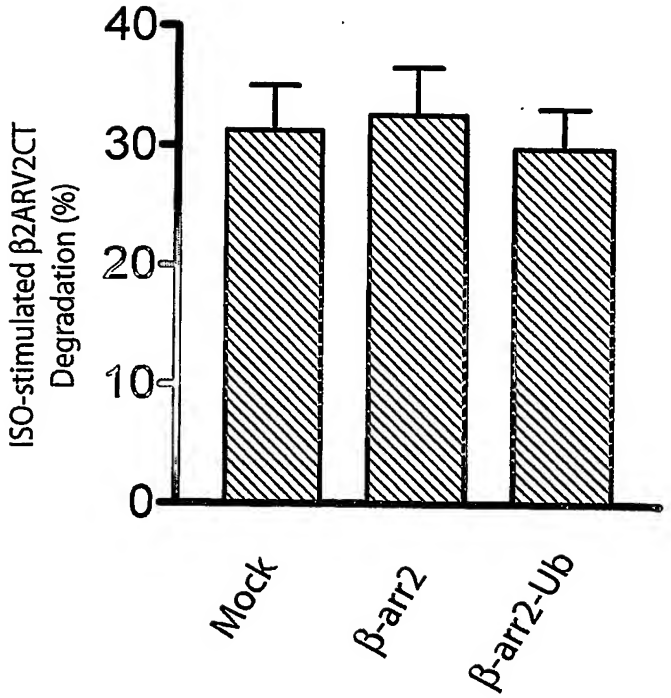

40
30
20
10
0
ISO-stimulated β2ARV2CT Degradation (%)
Mock
β-arr2
β-arr2-Ub

Fig.8

EYFP-BARR2-Ub

```
661/221                                                 691/231
CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC
L   L   E   F   V   T   A   A   G   I   T   L   G   M   D   E   L   Y   K   S
721/241                                                 751/251
GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCT GCA GTC GAC GGT ACC ACG CGC ACC
G   L   R   S   R   A   Q   A   S   K   S   A   V   D   G   T   T   R   T
1/1                                                     31/11
ATG GGT GAA AAA CCC GGG ACC AGG GTC TTC AAG AAG TCG AGC CCT AAC TGC AAG CTC ACC
M   G   E   K   P   G   T   R   V   F   K   K   S   S   P   N   C   K   L   T
61/21                                                   91/31
GTG TAC TTG GGC AAG CGT GAC TTT GTG GAT CAC TTG GAC AAA GTG GAT CCT GTC GAT GGT
V   Y   L   G   K   R   D   F   V   D   H   L   D   K   V   D   P   V   D   G
121/41                                                  151/51
GTG GTG CTT GTG GAT CCT GAC TAC TTG AAG GAC CGG AAA GTG TTT GTG ACC CTC ACC TGT
V   V   L   V   D   P   D   Y   L   K   D   R   K   V   F   V   T   L   T   C
181/61                                                  211/71
GCC TTC CGC TAT GGC CGA GAA GAC CTG GAT GTA CTG GGC CTG TCT TTC CGC AAA GAT CTG
A   F   R   Y   G   R   E   D   L   D   V   L   G   L   S   F   R   K   D   L
241/81                                                  271/91
TTC ATC GCC ACC TAC CAG GCC TTC CCC CCC ATG CCC AAC CCA CCT CGG CCC CCC ACC CGC
F   I   A   T   Y   Q   A   F   P   P   M   P   N   P   P   R   P   P   T   R
301/101                                                 331/111
CTA CAG GAC CGA CTG CTG AAG AAG TTG GGC CAG CAT GCC CAC CCC TTT TTT TTC ACA ATA
L   Q   D   R   L   L   K   K   L   G   Q   H   A   H   P   F   F   F   T   I
361/121                                                 391/131
CCC CAG AAT TTG CCT TGC TCC GTC ACA CTG CAG CCA GGA CCG GAG GAC ACA GGG AAG GCC
P   Q   N   L   P   C   S   V   T   L   Q   P   G   P   E   D   T   G   K   A
421/141                                                 451/151
TGT GGA GTA GAC TTT GAG ATT CGA GCC TTC TGT GCC AAA TCT ATA GAA GAA AAA AGC CAC
C   G   V   D   F   E   I   R   A   F   C   A   K   S   I   E   E   K   S   H
481/161                                                 511/171
AAA AGG AAC TCC GTG CGG CTT ATC ATC AGA AAG GTA CAG TTT GCT CCT GAG ACA CCC GGC
K   R   N   S   V   R   L   I   I   R   K   V   Q   F   A   P   E   T   P   G
541/181                                                 571/191
CCC CAG CCA TCA GCT GAA ACC ACA CGC CAC TTC CTC ATG TCT GAC CGG AGG TCC CTG CAC
P   Q   P   S   A   E   T   T   R   H   F   L   M   S   D   R   R   S   L   H
601/201                                                 631/211
CTA GAG GCT TCC CTG GAC AAA GAG CTG TAC TAC CAT GGG GAA CCC CTC AAT GTC AAC GTC
L   E   A   S   L   D   K   E   L   Y   Y   H   G   E   P   L   N   V   N   V
661/221                                                 691/231
CAC GTC ACC AAC AAT TCT GCC AAG ACC GTC AAG AAG ATC AGA GTG TCT GTG AGA CAG TAT
H   V   T   N   N   S   A   K   T   V   K   K   I   R   V   S   V   R   Q   Y
721/241                                                 751/251
GCC GAC ATT TGC CTC TTC AGC ACC GCG CAG TAC AAG TGT CCT GTG GCT CAG CTT GAA CAA
A   D   I   C   L   F   S   T   A   Q   Y   K   C   P   V   A   Q   L   E   Q
781/261                                                 811/271
GAT GAC CAG GTG TCT CCC AGT TCC ACA TTC TGC AAG GTG TAC ACC ATA ACC CCG CTG CTC
D   D   Q   V   S   P   S   S   T   F   C   K   V   Y   T   I   T   P   L   L
841/281                                                 871/291
AGT GAC AAC CGA GAG AAG CGT GGC CTT GCC CTT GAT GGG CAA CTC AAG CAC GAA GAC ACC
S   D   N   R   E   K   R   G   L   A   L   D   G   Q   L   K   H   E   D   T
901/301                                                 931/311
AAC CTG GCT TCC AGC ACC ATT GTG AAG GAG GGA GCC AAC AAG GAG GTG CTG GGA ATC CTA
N   L   A   S   S   T   I   V   K   E   G   A   N   K   E   V   L   G   I   L
961/321                                                 991/331
GTA TCC TAC AGG GTC AAG GTG AAG CTG GTG GTG TCT CGA GGC GGG GAT GTC TCC GTG GAG
V   S   Y   R   V   K   V   K   L   V   V   S   R   G   G   D   V   S   V   E
1021/341                                                1051/351
CTA CCT TTC GTC CTA ATG CAC CCC AAG CCC CAC GAC CAC ATC ACC CTT CCC CGA CCC CAG
L   P   F   V   L   M   H   P   K   P   H   D   H   I   T   L   P   R   P   Q
1081/361                                                1111/371
TCA GCC CCC CGG GAA ATA GAC ATC CCT GTG GAT ACC AAC CTC ATT GAA TTC GAT ACC AAC
S   A   P   R   E   I   D   I   P   V   D   T   N   L   I   E   F   D   T   N
1141/381                                                1171/391
TAT GCC ACA GAC GAC GAC ATC GTG TTT GAG GAC TTT GCG AGG CTT CGG CTG AAG GGG ATG
Y   A   T   D   D   D   I   V   F   E   D   F   A   R   L   R   L   K   G   M
1201/401                                                1231/410
```

```
AAG GAT GAC GAC TGT GAT GAC CAG TTC TGC GTC GAC CAG ATC TTC GTG AAG ACT CTG
K   D   D   D   C   D   D   Q   F   C   V   D   Q   I   F   V   K   T   L
22/8                                52/18
ACT GGT AAG ACC ATC ACC CTC GAG GTG GAG CCC AGT GAC ACC ATC GAG AAT GTC AAG GCA
T   G   K   T   I   T   L   E   V   E   P   S   D   T   I   E   N   V   K   A
82/28                               112/38
AAG ATC CAA GAT AAG GAA GGC ATT CCT CCT GAT CAG CAG AGG TTG ATC TTT GCC GGA AAA
K   I   Q   D   K   E   G   I   P   P   D   Q   Q   R   L   I   F   A   G   K
142/48                              172/58
CAG CTG GAA GAT GGT CGT ACC CTG TCT GAC TAC AAC ATC CAG AAA GAG TCC ACC TTG CAC
Q   L   E   D   G   R   T   L   S   D   Y   N   I   Q   K   E   S   T   L   H
202/68
CTG GTA CTC CGT CTC AGA GGT GGG TGA
L   V   L   R   L   R   G   G   ***
```

Fig. 9

EYFP-BARR2-Ub48

```
661/221                                                 691/231
CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC
L   L   E   F   V   T   A   A   G   I   T   L   G   M   D   E   L   Y   K   S
721/241                                                 751/251
GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCT GCA GTC GAC GGT ACC ACG CGC ACC
G   L   R   S   R   A   Q   A   S   K   S   A   V   D   G   T   T   R   T
1/1                                                     31/11
ATG GGT GAA AAA CCC GGG ACC AGG GTC TTC AAG AAG TCG AGC CCT AAC TGC AAG CTC ACC
M   G   E   K   P   G   T   R   V   F   K   K   S   S   P   N   C   K   L   T
61/21                                                   91/31
GTG TAC TTG GGC AAG CGT GAC TTT GTG GAT CAC TTG GAC AAA GTG GAT CCT GTC GAT GGT
V   Y   L   G   K   R   D   F   V   D   H   L   D   K   V   D   P   V   D   G
121/41                                                  151/51
GTG GTG CTT GTG GAT CCT GAC TAC TTG AAG GAC CGG AAA GTG TTT GTG ACC CTC ACC TGT
V   V   L   V   D   P   D   Y   L   K   D   R   K   V   F   V   T   L   T   C
181/61                                                  211/71
GCC TTC CGC TAT GGC CGA GAA GAC CTG GAT GTA CTG GGC CTG TCT TTC CGC AAA GAT CTG
A   F   R   Y   G   R   E   D   L   D   V   L   G   L   S   F   R   K   D   L
241/81                                                  271/91
TTC ATC GCC ACC TAC CAG GCC TTC CCC CCC ATG CCC AAC CCA CCT CGG CCC CCC ACC CGC
F   I   A   T   Y   Q   A   F   P   P   M   P   N   P   P   R   P   P   T   R
301/101                                                 331/111
CTA CAG GAC CGA CTG CTG AAG AAG TTG GGC CAG CAT GCC CAC CCC TTT TTT TTC ACA ATA
L   Q   D   R   L   L   K   K   L   G   Q   H   A   H   P   F   F   F   T   I
361/121                                                 391/131
CCC CAG AAT TTG CCT TGC TCC GTC ACA CTG CAG CCA GGA CCG GAG GAC ACA GGG AAG GCC
P   Q   N   L   P   C   S   V   T   L   Q   P   G   P   E   D   T   G   K   A
421/141                                                 451/151
TGT GGA GTA GAC TTT GAG ATT CGA GCC TTC TGT GCC AAA TCT ATA GAA GAA AAA AGC CAC
C   G   V   D   F   E   I   R   A   F   C   A   K   S   I   E   E   K   S   H
481/161                                                 511/171
AAA AGG AAC TCC GTG CGG CTT ATC ATC AGA AAG GTA CAG TTT GCT CCT GAG ACA CCC GGC
K   R   N   S   V   R   L   I   I   R   K   V   Q   F   A   P   E   T   P   G
541/181                                                 571/191
CCC CAG CCA TCA GCT GAA ACC ACA CGC CAC TTC CTC ATG TCT GAC CGG AGG TCC CTG CAC
P   Q   P   S   A   E   T   T   R   H   F   L   M   S   D   R   R   S   L   H
601/201                                                 631/211
CTA GAG GCT TCC CTG GAC AAA GAG CTG TAC TAC CAT GGG GAA CCC CTC AAT GTC AAC GTC
L   E   A   S   L   D   K   E   L   Y   Y   H   G   E   P   L   N   V   N   V
661/221                                                 691/231
CAC GTC ACC AAC AAT TCT GCC AAG ACC GTC AAG AAG ATC AGA GTG TCT GTG AGA CAG TAT
H   V   T   N   N   S   A   K   T   V   K   K   I   R   V   S   V   R   Q   Y
721/241                                                 751/251
GCC GAC ATT TGC CTC TTC AGC ACC GCG CAG TAC AAG TGT CCT GTG GCT CAG CTT GAA CAA
A   D   I   C   L   F   S   T   A   Q   Y   K   C   P   V   A   Q   L   E   Q
781/261                                                 811/271
GAT GAC CAG GTG TCT CCC AGT TCC ACA TTC TGC AAG GTG TAC ACC ATA ACC CCG CTG CTC
D   D   Q   V   S   P   S   S   T   F   C   K   V   Y   T   I   T   P   L   L
841/281                                                 871/291
AGT GAC AAC CGA GAG AAG CGT GGC CTT GCC CTT GAT GGG CAA CTC AAG CAC GAA GAC ACC
S   D   N   R   E   K   R   G   L   A   L   D   G   Q   L   K   H   E   D   T
901/301                                                 931/311
AAC CTG GCT TCC AGC ACC ATT GTG AAG GAG GGA GCC AAC AAG GAG GTG CTG GGA ATC CTA
N   L   A   S   S   T   I   V   K   E   G   A   N   K   E   V   L   G   I   L
961/321                                                 991/331
GTA TCC TAC AGG GTC AAG GTG AAG CTG GTG GTG TCT CGA GGC GGG GAT GTC TCC GTG GAG
V   S   Y   R   V   K   V   K   L   V   V   S   R   G   G   D   V   S   V   E
1021/341                                                1051/351
CTA CCT TTC GTC CTA ATG CAC CCC AAG CCC CAC GAC CAC ATC ACC CTT CCC CGA CCC CAG
L   P   F   V   L   M   H   P   K   P   H   D   H   I   T   L   P   R   P   Q
1081/361                                                1111/371
TCA GCC CCC CGG GAA ATA GAC ATC CCT GTG GAT ACC AAC CTC ATT GAA TTC GAT ACC AAC
S   A   P   R   E   I   D   I   P   V   D   T   N   L   I   E   F   D   T   N
1141/381                                                1171/391
TAT GCC ACA GAC GAC GAC ATC GTG TTT GAG GAC TTT GCG AGG CTT CGG CTG AAG GGG ATG
Y   A   T   D   D   D   I   V   F   E   D   F   A   R   L   R   L   K   G   M
1201/401                                                1231/410
```

```
AAG GAT GAC GAC TGT GAT GAC CAG TTC TGC GTC GAC CAG ATT TTC GTC AAG ACT TTG
K   D   D   D   C   D   D   Q   F   C   V   D   Q   I   F   V   K   T   L
22/8                                52/18
ACC GGT AAA ACC ATA ACA TTG GAA GTT GAA TCT TCC GAT ACC ATC GAC AAC GTT AAG TCG
T   G   K   T   I   T   L   E   V   E   S   S   D   T   I   E   N   V   K   S
82/28                               112/38
AAA ATT CAA GAC AAG GAA GGT ATC CCT CCA GAT CAA CAA AGA TTG ATC TTT GCC GGT AGG
K   I   Q   D   K   E   G   I   P   P   D   Q   Q   R   L   I   F   A   G   R
142/48                              172/58
CAG CTA GAA GAC GGT AGA ACG CTG TCT GAT TAC AAC ATT CAG AAG GAG TCC ACC TTA CAT
Q   L   E   D   G   R   T   L   S   D   Y   N   I   Q   K   E   S   T   L   H
202/68
CTT GTG CTA AGG CTA AGA GGT GGT TGA
L   V   L   R   L   R   G   G   ***
```

Fig. 10

EGFP-BARR2-Ub48

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661/221                                          691/231
CTG CTG GAG TTC GTG ACC GCC GCC GGG ATC ACT CTC GGC ATG GAC GAG CTG TAC AAG TCC
L   L   E   F   V   T   A   A   G   I   T   L   G   M   D   E   L   Y   K   S
721/241                                          751/251
GGA CTC AGA TCT CGA GCT CAA GCT TCG AAT TCT GCA GTC GAC GGT ACC ACG CGC ACC
G   L   R   S   R   A   Q   A   S   K   S   A   V   D   G   T   T   R   T
1/1                                              31/11
ATG GGT GAA AAA CCC GGG ACC AGG GTC TTC AAG AAG TCG AGC CCT AAC TGC AAG CTC ACC
M   G   E   K   P   G   T   R   V   F   K   K   S   S   P   N   C   K   L   T
61/21                                            91/31
GTG TAC TTG GGC AAG CGT GAC TTT GTG GAT CAC TTG GAC AAA GTG GAT CCT GTC GAT GGT
V   Y   L   G   K   R   D   F   V   D   H   L   D   K   V   D   P   V   D   G
121/41                                           151/51
GTG GTG CTT GTG GAT CCT GAC TAC TTG AAG GAC CGG AAA GTG TTT GTG ACC CTC ACC TGT
V   V   L   V   D   P   D   Y   L   K   D   R   K   V   F   V   T   L   T   C
181/61                                           211/71
GCC TTC CGC TAT GGC CGA GAA GAC CTG GAT GTA CTG GGC CTG TCT TTC CGC AAA GAT CTG
A   F   R   Y   G   R   E   D   L   D   V   L   G   L   S   F   R   K   D   L
241/81                                           271/91
TTC ATC GCC ACC TAC CAG GCC TTC CCC CCC ATG CCC AAC CCA CCT CGG CCC CCC ACC CGC
F   I   A   T   Y   Q   A   F   P   P   M   P   N   P   P   R   P   P   T   R
301/101                                          331/111
CTA CAG GAC CGA CTG CTG AAG AAG TTG GGC CAG CAT GCC CAC CCC TTT TTT TTC ACA ATA
L   Q   D   R   L   L   K   K   L   G   Q   H   A   H   P   F   F   F   T   I
361/121                                          391/131
CCC CAG AAT TTG CCT TGC TCC GTC ACA CTG CAG CCA GGA CCG GAG GAC ACA GGG AAG GCC
P   Q   N   L   P   C   S   V   T   L   Q   P   G   P   E   D   T   G   K   A
421/141                                          451/151
TGT GGA GTA GAC TTT GAG ATT CGA GCC TTC TGT GCC AAA TCT ATA GAA GAA AAA AGC CAC
C   G   V   D   F   E   I   R   A   F   C   A   K   S   I   E   E   K   S   H
481/161                                          511/171
AAA AGG AAC TCC GTG CGG CTT ATC ATC AGA AAG GTA CAG TTT GCT CCT GAG ACA CCC GGC
K   R   N   S   V   R   L   I   I   R   K   V   Q   F   A   P   E   T   P   G
541/181                                          571/191
CCC CAG CCA TCA GCT GAA ACC ACA CGC CAC TTC CTC ATG TCT GAC CGG AGG TCC CTG CAC
P   Q   P   S   A   E   T   T   R   H   F   L   M   S   D   R   R   S   L   H
601/201                                          631/211
CTA GAG GCT TCC CTG GAC AAA GAG CTG TAC TAC CAT GGG GAA CCC CTC AAT GTC AAC GTC
L   E   A   S   L   D   K   E   L   Y   Y   H   G   E   P   L   N   V   N   V
661/221                                          691/231
CAC GTC ACC AAC AAT TCT GCC AAG ACC GTC AAG AAG ATC AGA GTG TCT GTG AGA CAG TAT
H   V   T   N   N   S   A   K   T   V   K   K   I   R   V   S   V   R   Q   Y
721/241                                          751/251
GCC GAC ATT TGC CTC TTC AGC ACC GCG CAG TAC AAG TGT CCT GTG GCT CAG CTT GAA CAA
A   D   I   C   L   F   S   T   A   Q   Y   K   C   P   V   A   Q   L   E   Q
781/261                                          811/271
GAT GAC CAG GTG TCT CCC AGT TCC ACA TTC TGC AAG GTG TAC ACC ATA ACC CCG CTG CTC
D   D   Q   V   S   P   S   S   T   F   C   K   V   Y   T   I   T   P   L   L
841/281                                          871/291
AGT GAC AAC CGA GAG AAG CGT GGC CTT GCC CTT GAT GGG CAA CTC AAG CAC GAA GAC ACC
S   D   N   R   E   K   R   G   L   A   L   D   G   Q   L   K   H   E   D   T
901/301                                          931/311
AAC CTG GCT TCC AGC ACC ATT GTG AAG GAG GGA GCC AAC AAG GAG GTG CTG GGA ATC CTA
N   L   A   S   S   T   I   V   K   E   G   A   N   K   E   V   L   G   I   L
961/321                                          991/331
GTA TCC TAC AGG GTC AAG GTG AAG CTG GTG GTG TCT CGA GGC GGG GAT GTC TCC GTG GAG
V   S   Y   R   V   K   V   K   L   V   V   S   R   G   G   D   V   S   V   E
1021/341                                         1051/351
CTA CCT TTC GTC CTA ATG CAC CCC AAG CCC CAC GAC CAC ATC ACC CTT CCC CGA CCC CAG
L   P   F   V   L   M   H   P   K   P   H   D   H   I   T   L   P   R   P   Q
1081/361                                         1111/371
TCA GCC CCC CGG GAA ATA GAC ATC CCT GTG GAT ACC AAC CTC ATT GAA TTC GAT ACC AAC
S   A   P   R   E   I   D   I   P   V   D   T   N   L   I   E   F   D   T   N
1141/381                                         1171/391
TAT GCC ACA GAC GAC GAC ATC GTG TTT GAG GAC TTT GCG AGG CTT CGG CTG AAG GGG ATG
Y   A   T   D   D   D   I   V   F   E   D   F   A   R   L   R   L   K   G   M
1201/401                                         1231/410
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AAG GAT GAC GAC TGT GAT GAC CAG TTC TGC GTC GAC CAG ATC TTC GTG AAG ACT CTG
K   D   D   D   C   D   D   Q   F   C   V   D   Q   I   F   V   K   T   L
22/8                                52/18
ACT GGT AAG ACC ATC ACC CTC GAG GTG GAG CCC AGT GAC ACC ATC GAG AAT GTC AAG GCA
T   G   K   T   I   T   L   E   V   E   P   S   D   T   I   E   N   V   K   A
82/28                               112/38
AAG ATC CAA GAT AAG GAA GGC ATT CCT CCT GAT CAG CAG AGG TTG ATC TTT GCC GGA AGA
K   I   Q   D   K   E   G   I   P   P   D   Q   Q   R   L   I   F   A   G   R
142/48                              172/58
CAG CTG GAA GAT GGT CGT ACC CTG TCT GAC TAC AAC ATC CAG AAA GAG TCC ACC TTG CAC
Q   L   E   D   G   R   T   L   S   D   Y   N   I   Q   K   E   S   T   L   H
202/68
CTG GTA CTC CGT CTC AGA GGT GGG TGA
L   V   L   R   L   R   G   G   ***
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Fig. 11A Human G Protein Coupled Receptor Family
(Receptors known as of January, 1999)

CLASS	LIGAND	NUMBER	TISSUE	PHYSIOLOGY	THERAPEUTICS
•Class I					
Rhodopsin like					
	•Amine				
	·Acetylcholine				
	(muscarinic & nicotinic)	5	Brain, Nerves, Heart	Neurotransmitter	Acuity, Alzheimer's
	·Adrenoceptors				
	·Alpha Adrenoceptors	6	Brain, Kidney, Lung	Gluconeogenesis	Diabetes, Cardiovascular
	·Beta Adrenoceptors	3	Kidney, Heart	Muscle Contraction	Cardiovascular, Respiratory
	·Dopamine	5	Brain, Kidney, GI	Neurotransmitter	Cardiovascular, Parkinson's
	·Histamine	2	Vascular, Heart, Brain	Vascular Permeability	Anti-inflammatory, Ulcers
	·Serotonin (5-HT)	16	Most Tissues	Neurotransmitter	Depression, Insomnia, Analgesic
	•Peptide				
	·Angiotensin	2	Vascular, Liver, Kidney	Vasoconstriction	Cardiovascular, Endocrine
	·Bradykinin	1	Liver, Blood	Vasodilation,	Anti-inflammatory, Asthma
	·C5a anaphylatoxin	1	Blood	Immune System	Anti-inflammatory
	·Fmet-leu-phe	3	Blood	Chemoattractant	Anti-inflammatory
	·Interleukin-8	1	Blood	Chemoattractant	Anti-inflammatory
	·Chemokine	6	Blood	Chemoattractant	Anti-inflammatory
	·Orexin	2	Brain	Fat Metabolism	Obesity
	·Nociceptin	1	Brain	Bronchodilator, Pain	Airway Diseases, Anesthetic
	·CCK (Gastrin)	2	Gastrointestinal	Motility, Fat Absorption	Gastrointestinal, Obesity, Parkinson's
	·Endothelin	2	Heart, Bronchus, Brain	Muscle Contraction	Cardiovascular, Respiratory
	·Melanocortin	5	Kidney, Brain	Metabolic Regulation	Anti-inflammatory, Analgesics
	·Neuropeptide Y	5	Nerves, Intestine, Blood	Neurotransmitter	Behavior, Memory, Cardio-vascular
	·Neurotensin	1	Brain,	CNS	Cardiovascular, Analgesic

·Opioid	3	Brain,	CNS	Depression, Analgesic
·Somatostatin	5	Brain, Gastrointestinal	Neurotransmitter	Oncology, Alzheimer's
·Tachykinin				
(Substance P, NKA_1)	3	Brain Nerves	Neurohormone	Depression, Analgesic
·Thrombin	3	Platelets, Blood Vessels	Coagulation	Anti-coagulant, Anti-inflammatory
·Vasopressin-like	4	Arteries, Heart, Bladder	Water Balance	Anti-diuretic, Diabetic Complications
·Galanin	1	Brain, Pancreas	Neurotransmitter	Analgesics, Alzheimer's
·Hormone protein				
·Follicle stimulating hormone	1	Ovary, Testis	Endocrine	Infertility
·Lutropin-choriogonadotropic	1	Ovary, Testis	Endocrine	Infertility
·Thyrotropin	1	Thyroid	Endocrine	Thyroidism, Metabolism
·(Rhod)opsin				
·Opsin	5	Eye	Photoreception	Ophthalmic Diseases
·Olfactory	4(~1000)	Nose	Smell	Olfactory Diseases
·Prostanoid				
·Prostaglandin	5	Arterial, Gastrointestinal	Vasodilation, Pain	Cardiovascular, Analgesic
·Lysophosphatidic Acid	2	Vessels, Heart, Lung	Inflammation	Cancer, Anti-Inflammatory
·Sphingosine-1-phosphate	2	Most Cells	Cell proliferation	Cancer
·Leukotriene	1	White Blood Cells, Bronchus	Inflammation	Asthma, Rheumatoid Arthritis
·Prostacyclin	1	Arterial, Gastrointestinal	Platelet Regulation	Cardiovascular
·Thromboxane	1	Arterial, Bronchus	Vasoconstriction	Cardiovascular, Respiratory
·Nucleotide-like				
·Adenosine	4	Vascular, Bronchus	Multiple Effects	Cardiovascular, Respiratory
·Purinoceptors	4	Vascular, Platelets	Relaxes Muscle	Cardiovascular, Respiratory
·Cannabis	2	Brain	Sensory Perception	Analgesics, Memory
·Platelet activating factor	1	Most Peripheral Tissues	Inflammation	Anti-inflammatory, Anti-asthmatic

	·Gonadotropin-releasing hormone like				
	·Gonadotropin-releasing hormone	1	Reproductive Organs, Pituitary	Reproduction	Prostate Cancer, Endometriosis
	·Thyrotropin-releasing hormone	1	Pituitary, Brain	Thyroid Regulation	Metabolic Regulation
	·Growth hormone- inhibiting factor	1	Gastrointestinal	Neuroendocrine	Oncology, Alzheimer's
	·Melatonin	1	Brain, Eye, Pituitary	Neuroendocrine	Regulation of Circadian Cycle
•Class II Secretin like					
	·Secretin	1	Gastrointestinal, Heart	Digestion	Obesity, Gastrointestinal
	·Calcitonin	1	Bone, Brain	Calcium Resorption	Osteoporosis
	·Corticotropin releasing factor/urocortin	1	Adrenal, Vascular, Brain	Neuroendocrine	Stress, Mood, Obesity
	·Gastric inhibitory peptide (GIP)	1	Adrenals, Fat Cells	Sugar/Fat Metabolism	Diabetes, Obesity
	·Glucagon	1	Liver, Fat Cells, Heart	Gluconeogenesis	Cardiovascular
	·Glucagon-like Peptide 1 (GLP-1)	1	Pancreas, Stomach, Lung	Gluconeogenesis	Cardiovascular, Diabetes, Obesity
	·Growth hormone-releasing hormone		Brain	Neuroendocrine	Growth Regulation
	·Parathyroid hormone	1	Bone, Kidney	Calcium Regulation	Osteoporosis
	·PACAP	1	Brain, Pancreas, Adrenals	Metabolism	Metabolic Regulation
	·Vasoactive intestinal polypeptide (VIP)	1	Gastrointestinal	Motility	Gastrointestinal
•Class III					
	·Metabotropic Glutamate	7	Brain	Sensory Perception	Hearing, Vision
	·$GABA_B$	1	Brain	Neurotransmitter	Mood Disorders
	·Extracellular Calcium Sensing	1	Parathyroid, Kidney, GI Tract	Calcium Regulation	Cataracts, GI Tumors

Fig. 11B

G protein-coupled receptors:

(Division into Class A
Or Class B)

1. **A1 adenosine receptor** [Homo sapiens]. ACCESSION AAB25533
npivyaf riqkfrvtfl kiwndhfrcq pappidedlp eerpdd
Class A

2. **adrenergic, alpha -1B-, receptor** [Homo sapiens]. ACCESSION NP_000670
npiiypcsskefkrafvrilgcqcrgrgrrrrrrrrrlggcaytyrpwtrggslersqsrkdslddsgsclsgsqrtlpsaspspgylgr gapppvelcafpewkapgallslpapeppgrrgrhdsgplftfkllltepespgtdggasnggceaaadvangqpgfksnmpla pgqf
Class A

3. **adrenergic receptor alpha-2A** [Homo sapiens]. ACCESSION AAG00447
npviytifnhdfrrafkkilcrgdrkriv
Class A

4. **alpha-2B-adrenergic receptor** - human. ACCESSION A37223
npviytifnqdfrrafrrilcrpwtqtaw
Class A

5. **alpha-2C-adrenergic receptor** - human. ACCESSION A31237
npviytvfnqdfrpsfkhilfrrrrrgfrq
Class A

6. **beta-1-adrenergic receptor** [Homo sapiens]. ACCESSION NP_000675
npiiycrspdfrkafqgllccarraarrrhathgdrprasgclarpgpppspgaasddddddvvgatpparllepwagcnggaa adsd ssldepcrpgfaseskv
Class A

7. **beta-2 adrenergic receptor.** ACCESSION P07550
npliycrspdfriafqellclrrsslkaygngyssngntgeqsgyhveqekenkllcedlpgtedfvghqgtvpsdnidsqgrncs tndsll
Class A

8. **dopamine receptor D1** [Homo sapiens]. ACCESSION NP_000785
npiiyafnadfrkafstllgcyrlcpatnnaietvsinnngaamfsshheprgsiskecnlvyliphavgssedlkkeeaagiarpl eklspalsvildydtdvslekiqpitqngqhpt
Class A

9. **D(2) dopamine receptor.** ACCESSION P14416
npiiyttfniefrkaflkilhc
Class A

10. **d3 dopamine receptor** - human. ACCESSION G01977
npviyttfniefrkaflkilsc
Class A

11. **dopamine receptor D4** - human. ACCESSION DYHUD4
npviytvfnaefrnvfrkalracc
Class A

12. **dopamine receptor D5** - human. ACCESSION DYHUD5
npviyafnadfqkvfaqllgcshfcsrtpvetvnisnelisynqdivfhkeiaaayihmmpnavtpgnrevdndeeegpfdrm
fqiyqtspdgdpvaesvweldcegeisldkitpftpngfh
Class A

13. **muscarinic acetylcholine receptor M1** [Homo sapiens]. ACCESSION NP_000729
npmcyalcnkafrdtfrllllcrwdkrrwrkipkrpgsvhrtpsrqc
Class A

14. **muscarinic acetylcholine receptor M2** [Homo sapiens]. ACCESSION NP_000730
npacyalcnatfkktfkhllmchyknigatr
Class A

15. **muscarinic acetylcholine receptor M3 [Homo sapiens].**
npvcyalcnktfrttfkmlllcqcdkkkrrkqqyqqrqsvifhkrapeqal
Class A

16. **muscarinic acetylcholine receptor M4** [Homo sapiens]. ACCESSION NP_000732
npacyalcnatfkktfrhlllcqymigtar
Class A

17. **m5 muscarinic receptor.** locus HUMACHRM ACCESSION AAA51569
npicyalcnrtfrktfkmlllcrwkkkkveeklywqgnsklp
Class A

18. **5-hydroxytryptamine (serotonin) receptor 1A** [Homo sapiens]. ACCESSION BAA90449
npviyayfnkdfqnafkkiikckf
Class A

19. **5-hydroxytryptamine (serotonin) receptor 1B** [Homo sapiens]. ACCESSION BAA94455
npiiytmsnedfkqafhklirfkcts
Class A

20. **5-hydroxytryptamine (serotonin) receptor 1E** [Homo sapiens]. ACCESSION BAA94458
npllytsfnedfklafkklircre
Class A

21. **OLFACTORY RECEPTOR 6A1.** ACCESSION O95222
npiiyclrnqevkralccilhlyqhqdpdpkkgsrnv
Class A

22. **OLFACTORY RECEPTOR 2C1.** ACCESSION O95371
npliytlrnmevkgalrrllgkgrevg
Class A

23. **angiotensin receptor 1 [Homo sapiens].** ACCESSION NP_033611
nplfygflgkkfkryflqllkyippkakshsnlstkmstlsyrpsdnvssstkkpapcfeve
Class B

24. **angiotensin receptor 2** [Homo sapiens]. ACCESSION NP_000677
npflycfvgnrfqqklrsvfrvpitwlqgkresmscrkssslremetfvs
Class B

25. **interleukin 8 receptor beta (CXCR2)** [Homo sapiens]. ACCESSION NM_001557
NPLIYAFIGQKFRHGLLKILAIHGLISKDSLPKDSRPSFVGSSSGHTSTTL
Class B

26. **cx3c chemokine receptor 1** (cx3cr1) (fractalkine receptor)
ACCESSION P49238
npliyafagekfrrylyhlygkclavlcgrsvhvdfsssesqrsrhgsvlssnftyhtsdgdallll
Class B

27. **neurotensin receptor - human.** ACCESSION S29506
n pilynlvsanfrhiflatlaclcpvwrrrrkrpafsrkadsvssnhtlssnatretly
Class B

28. **SUBSTANCE-P RECEPTOR (SPR)** (NK-1 RECEPTOR) (NK-1R). ACCESSION P25103
npiiyccIndrfrlgfkhafrccpfisagdyeglemkstrylqtqgsvykvsrlettistvvgaheeepedgpkatpssldltsncssrsdskt
mtesfsfssnvls
Class B

29. **vasopressin receptor type 2** [Homo sapiens]. ACCESSION AAD16444
npwiyasfsssvsselrsllccargrtppslgpqdesctttassslakdtss
Class B

30. **thyrotropin-releasing hormone receptor** - human. ACCESSION JN0708
npviynlmsqkfraafrklcnckqkptekpanysvalnysvikesdhfsteldditytdtylsatkvsfddtclasevsfsqs
Class B

31. **oxytocin receptor - human.** ACCESSION A55493
npwiymlftghlfhelvqrflccsasylkgrrlgetsaskksnsssfvlshrsssqrscsqpsta
Class B

32. **neuromedin U receptor 1 [Homo sapiens].** ACCESSION AAG24793
npvlyslmssrfretfqealclgacchrlrprhsshslsrmttgstlcdvgslgswvhplagndgpeaqqetdps
Class B

33. **gastrin receptor.** ACCESSION AAC37528
nplvycfmhrrfrqacletcarccprpprarpralpdedpptpsiaslsrlsyttistlgpg
Class B

34. **galanin receptor 3 [Homo sapiens].** ACCESSION 10879541
nplvyalasrhfrarfrrlwpcgrrrrhrarralrrvrpassgppgcpgdarpsgrllagggqgpepregpvhggeaargpe
Class A

35. **edg-1** - human. ACCESSION A35300
npiiytltnkemrrafirimscckcpsgdsagkfkrpiiagmefsrsksdnsshpqkdegdnpetimssgnvnsss
Class A

36. **central cannabinoid receptor** [Homo sapiens]. ACCESSION NP_057167
npiiyalrskdlrhafrsmfpscegtaqpldnsmgdsdclhkhannaasvhraaescikstvkiakvtmsvstdtsaeal
Class A

37. **delta opioid receptor** - human. ACCESSION I38532
npvlyafldenfkrcfrqlcrkpcgrpdpssfsrpreatarervtactpsdgpgggraa
Class A

38. **proteinase activated receptor 2 (PAR-2) human.** ACCESSION P55085
dpfvyyfvshdfrdhaknallcrsvrtvkqmqvsltskkhsrksssysssstttvktsy
Class B

39. **vasopressive intestinal peptide receptor (VIPR) rat.** ACCESSION NM_012685
NGEVQAELRRKWRRWHLQGVLGWSSKSQHPWGGSNGATCSTQVSMLTRVSPSA
RRSSSFQAEVSLV
Class B